

WHAT IS CLAIMED IS:

1. A composition comprising a plurality of positionally distinguishable sequence specific reagents attached to a solid substrate, which reagents are capable of specifically binding to a predetermined subunit sequence of a preselected multi-subunit length having at least three subunits, said reagents representing substantially all possible sequences of said preselected length.

10 2. A composition of Claim 1, wherein said subunit sequence is a polynucleotide or a polypeptide.

15 3. A composition of Claim 1, wherein said preselected multi-subunit length is five subunits and said subunit sequence is a polynucleotide sequence.

20 4. A composition of Claim 1, wherein said specific reagent is an oligonucleotide of at least about five nucleotides.

5. A composition of Claim 1, wherein said specific reagent is a monoclonal antibody.

25 6. A composition of Claim 1, wherein said specific reagents are all attached to a single solid substrate.

7. A composition of Claim 1, wherein said reagents comprise about 3000 different sequences.

8. A composition of Claim 1, wherein said reagents represents at least about 25% of the possible subsequences of said preselected length.

5 9. A composition of Claim 1, wherein said reagents are localized in regions of the substrate having a density of at least 25 regions per square centimeter.

10 10. A composition of Claim 6, wherein said substrate has a surface area of less than about 4 square centimeters.

11. A method of analyzing a sequence of a polynucleotide or a polypeptide, said method comprising the step of:

15 a) exposing said polynucleotide or polypeptide to a composition of Claim 1.

12. A method of identifying or comparing a target sequence with a reference, said method comprising the step of:

20 a) exposing said target sequence to a composition of Claim 1;

25 b) determining the pattern of positions of said reagents which specifically interact with said target sequence; and

c) comparing said pattern with the pattern exhibited by said reference when exposed to said composition.

13. A method for sequencing a segment of a
polynucleotide comprising the steps of:

a) combining:

- i) a substrate comprising a plurality of chemically synthesized and positionally distinguishable oligonucleotides capable of recognizing defined oligonucleotide sequences; and
- ii) a target polynucleotide; thereby forming high fidelity matched duplex structures of complementary subsequences of known sequence; and

b) determining which of said reagents have specifically interacted with subsequences in said target polynucleotide.

14. A method of Claim 13, wherein said segment is substantially the entire length of said polynucleotide.

15. A method for sequencing a polymer, said method comprising the steps of:

a) preparing a plurality of reagents which each specifically bind to a subsequence of preselected length;

b) positionally attaching each of said reagents to one or more solid phase substrates, thereby producing substrates of

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positionally definable sequence specific
probes;

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c) combining said substrates with a target
polymer whose sequence is to be determined;
and
d) determining which of said reagents have
specifically interacted with subsequences
in said target polymer.

10 16. A method of Claim 15, wherein said substrates
are beads.

15 17. A method of Claim 15, wherein said plurality of
reagents comprise substantially all possible subsequences of
said preselected length found in said target.

20 18. A method of Claim 15, wherein said solid phase
substrates are a single substrate having attached thereto
reagents recognizing substantially all possible subsequences of
preselected length found in said target.

25 19. A method of Claim 15, further comprising the
step of analyzing a plurality of said recognized subsequences
to assemble a sequence of said target polymer.

20. A method of Claim 16, wherein at least some of
said plurality of substrates have one subsequence specific
reagent attached thereto, and said substrates are coded to
indicate the specificity of said reagent.

21. A method of using a fluorescent nucleotide to detect interactions with oligonucleotide probes of known sequence, said method comprising:

- 5 a) attaching said nucleotide to a target unknown polynucleotide sequence, and
- b) exposing said target polynucleotide sequence to a collection of positionally defined oligonucleotide probes of known sequences to determine the sequences of said probes which interact with said target.

22. A method of Claim 21, further comprising the

15 step of:

- a) collating said known sequences to determine the overlaps of said known sequences to determine the sequence of said target sequence.

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23. A method of mapping a plurality of sequences relative to one another, said method comprising:

- 25 a) preparing a substrate having a plurality of positionally attached sequence specific probes are attached;
- b) exposing each of said sequences to said substrate, thereby determining the patterns of interaction between said sequence specific probes and said sequences; and

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c) determining the relative locations of said sequence specific probe interactions on said sequences to determine the overlaps and order of said sequences.

10 24. A method of claim 23, wherein said sequence specific probes are oligonucleotides.

15 25. A method of claim 23, wherein said sequences are nucleic acid sequences.

20 26. A method of preparing sequences on a substrate comprising the steps of:

- a) exposing a first region of said substrate to an activator to remove a protective group;
- b) exposing at least said first region to a first monomer;
- c) exposing a second region to an activator to remove a protective group; and
- d) exposing at least said second region to a second monomer.

25 27. The method as recited in claim 26 wherein said steps of exposing to an activator use an activator selected from the group consisting of ion beams, electron beams, gamma rays, x-rays, ultra-violet radiation, light, infra-red radiation, microwaves, electric currents, radiowaves, and combinations thereof.

30 28. The method as recited in claim 26 wherein said protective groups are photosensitive protective groups.

29. The method as recited in claim 26 wherein said steps of exposing to an activator are steps of applying light to selected regions of said substrate.

30 30. The method as recited in claim 26 wherein said first and the second monomers are amino acids.

31. The method as recited in claim 26 further comprising a step of screening sequences on said substrate for affinity with a receptor, said step of screening further comprising the step of exposing said substrate to said receptor and testing for the presence of said receptor in said first and said second region.

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32. The method as recited in claim 31 wherein said receptor is an antibody.

10 33. The method as recited in claim 26 wherein said substrate is selected from the group consisting of polymerized Langmuir Blodgett film, functionalized glass,

germanium, silicon, polymers, (poly)tetrafluoro-ethylene, polystyrene, gallium arsenide, and combinations thereof.

15 34. The method as recited in claim 26 wherein said protective group is selected from the group consisting of ortho-nitrobenzyl derivatives, 6-nitroveratryloxy-carbonyl, 2-nitrobenzyloxy-car-bonyl, cinnamoyl derivatives, and mixtures thereof.

20 35. The method as recited in claim 26 wherein said first and second regions each have total areas of less than 1 cm².

25 36. The method as recited in claim 26 wherein said first and second regions each have total areas of between about 1 μm^2 and 10,000 μm^2 .

37. The method as recited in claim 29 wherein said light is monochromatic coherent light.

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38. The method as recited in claim 26 wherein said steps of exposing to an activator are carried out with a solution in contact with said substrate.

30 39. The method as recited in claim 38 wherein said solution further comprises said first or said second monomer.

40. The method as recited in claim 31 wherein said receptor further comprises a marker selected from the group consisting of radioactive markers and fluorescent

~~markers and wherein said step of testing for the presence of the receptor is a step of detecting said marker.~~

41 5 The method as recited in claim 26 wherein the steps of exposing to an activator further comprise steps of:

- a) placing a mask adjacent to said substrate, said mask having substantially transparent regions and substantially opaque regions at a wavelength of light; and
- b) illuminating said mask with a light source, said light source producing at least said wavelength of light.

10 42. The method as recited in claim 26 wherein said steps are repeated so as to synthesize 10^3 or more different sequences on said substrate.

15 43. The method as recited in claim 26 wherein said steps are repeated so as to synthesize 10^6 or more different sequences on said substrate.

44. A method of synthesizing a plurality of chemical sequences, said chemical sequences comprising at least a first and a second monomer, comprising the steps of:

20 a) at a first region on a substrate having at least a first and a second region, said first and said second region comprising a substrate protective group, activating said first region to remove said substrate protective group in said first region;

b) exposing said first monomer to said substrate, said first monomer further comprising a first monomer protective group, said first monomer binding at said first region;

25 c) activating said second region to remove said substrate protective group in said second region;

d) exposing said second monomer to said substrate, said second monomer further comprising a second monomer protective group, said second monomer binding at said second region;

30 e) activating said first region to remove said first monomer protective group;

f) exposing a third monomer to said substrate, said third monomer binding at said first region to produce a first sequence;

g) activating said second region to remove said second monomer protective group; and

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h) exposing a fourth monomer to said sub-strate, said fourth monomer binding at said second region to produce a second sequence, said second sequence different from said first sequence.

5 45. A method of synthesizing a plurality of chemical sequences, said chemical sequences comprising at least a first and a second monomer, comprising the steps of:

10 a) on a substrate having at least a first and a second region deactivating said first region to provide a first protective group in said first region;

15 b) exposing said first monomer to said substrate, said first monomer binding at said second region;

20 c) removing said protective group in said first region;

25 d) deactivating said second region to provide a second protective group in said second region;

30 e) exposing said second monomer to said substrate, said second monomer binding at said first region;

35 f) removing said protective group in said second region;

40 g) deactivating said first region to provide a protective group in said first region;

45 h) exposing a third monomer to said sub-strate, said third monomer binding at said second region to produce a first sequence;

50 i) removing said protective group in said first region; and

55 j) exposing a fourth monomer to said sub-strate, said fourth monomer binding at said first region to produce a second sequence, said second sequence different than said first sequence.

46. A method of synthesizing at least a first polymer sequence and a second polymer sequence on a substrate, said first polymer sequence having a different monomer sequence from said second polymer sequence, comprising the steps of:

30 a) inserting a first mask between said sub-strate and an energy source, said mask having first regions and second regions, said first regions permitting passage of energy from said source, said second regions blocking energy from said source;

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5 b) directing energy from said source at said substrate, said energy removing a protective group from first portions of said first polymer under said first regions of said first mask;

5 c) exposing a second portion of said first polymer to said substrate to create a first polymer sequence;

10 d) inserting a second mask between said sub-strate and said energy source, said second mask having first regions and second regions;

10 e) directing energy from said source at said substrate, said energy removing said protective group under said first regions of said second mask from first portions of said second polymer; and

15 f) exposing a second portion of said second polymer to said substrate, said second portion of said second polymer binding with said first portion of said second polymer to create a polymer 8second sequence.

15 47. The method as recited in claim 46 wherein said energy is selected from the group consisting of ion beams, electron beams, gamma rays, x-rays, ultra-violet radiation, light, infra-red radiation, microwaves, electric fields, radio-waves, and combinations thereof.

20 48. The method as recited in claim 44 wherein said protective groups are photosensi-tive protective groups.

25 49. The method as recited in claims 44 or 45 wherein said steps of activating and deactivating are steps of applying light to selected regions of said substrate.

25 50. The method as recited in claims 44 or 45 wherein said first and said second monomers are amino acids.

30 51. The method as recited in claims 44, 45 or 46 further comprising a step of screening said first and said second sequences for affinity with a first receptor, said step of screening further comprising a step of exposing said substrate to said first receptor and testing for the presence of said first receptor.

52. The method as recited in claim 51 wherein said step of screening is a step of screening with antibodies.

53. The method as recited in claims 44, 45 or 46 wherein said substrate is selected from the group consisting of a polymerized Langmuir Blodgett film, functionalized glass, germanium, silicon, polymers, (poly)tetrafluoro-ethylene, gallium arsenide, gallium phosphide, silicon oxide, silicon nitride and combinations thereof.

54. The method as recited in claim 44 wherein said protective group, said first monomer protective group, and said second monomer protective group are selected from the group consisting of ortho-nitrobenzyl derivatives, 6-nitroveratryloxycarbonyl, 2-nitrobenzyloxy-car-bonyl, and mixtures thereof.

55. The method as recited in claim 45 wherein said protective group is a cinnamate group.

56. The method as recited in claims 44 or 45 wherein said first and second regions each have total areas of less than 1 cm².

57. The method as recited in claims 44 or 45 wherein said first and second regions each have total areas of between about 1 μm² and 10,000 μm².

58. The method as recited in claim 49 wherein said light is monochromatic coherent light.

59. The method as recited in claim 44 wherein said steps of activating are carried out with a solution in contact with said substrate.

60. The method as recited in claim 59 wherein said solution further comprises a monomer.

61. The method as recited in claim 51 wherein said receptor further comprises a marker selected from the group consisting of radioactive markers and fluorescent markers and wherein said step of testing for the presence of the receptor is a step of detecting said marker.

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62. ~~The method as recited in claims 44 or 45 wherein two of said first, said second, said third, and said fourth monomers are the same monomers.~~

5 63. The method as recited in claim 46 wherein the step of inserting a second mask is a step of translating said first mask from a first position to a second position.

10 64. The method as recited in claim 66 wherein the step of inserting a second mask is a step of rotating said first mask.

15 65. The method as recited in claim 51 further comprising the step of exposing said substrate to a second, labeled receptor, said second, labeled receptor binding at multiple sites on said first receptor.

20 66. The method as recited in claim 65 wherein said first receptor is an antibody of a first animal species and said second receptor is an antibody derived from a second species and directed at said first species.

25 67. The method as recited in claim 44 wherein:

a) said first monomer protective group is removable upon exposure to a first wavelength of light;

b) said second monomer protective group is removable upon exposure to a second wavelength of light;

c) said step of activating said first region to remove said first monomer

30 25 protective group is a step of exposing substantially all of said substrate to said first wavelength of light; and

d) said step of activating said second region to remove said second monomer protective group is a step of exposing substantially all of said substrate to said second wavelength of light.

30 68. A method as recited in claims 44 or 46 wherein said protective groups ~~are of the form:~~

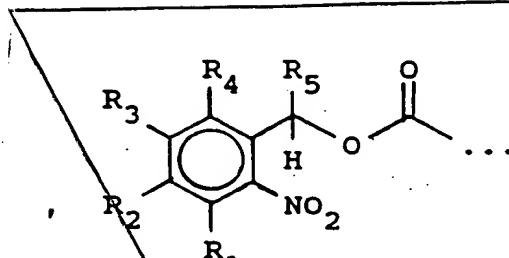
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where R₁ is alkoxy, alkyl, halo, aryl, alkenyl, or hydrogen; R₂ is alkoxy, alkyl, halo, aryl, nitro, or hydrogen; R₃ is alkoxy, alkyl, halo, nitro, aryl, or hydrogen; R₄ is alkoxy, alkyl, hydrogen, aryl, halo, or nitro; and R₅ is alkyl, alkynyl, cyano, alkoxy, hydrogen, halo, aryl, or alkenyl.

69. A method of screening a plurality of amino acid sequences for binding with a receptor comprising the steps of:

- a) on a glass plate having at least a first surface, said at least a first surface comprising a photoprotective material selected from the group consisting of nitroveratryloxy carbonyl and nitrobenzyloxy carbonyl, reacting said at least a first surface with t-butoxycarbonyl for storage, said glass plate substantially transparent to at least ultraviolet light;
- b) exposing said at least a first surface to TFA to remove said t-butoxycarbonyl;
- c) placing said glass plate on a reactor, said reactor comprising a reactor space, said at least a first surface exposed to said reactor space;
- d) placing a mask at a first position on said glass plate, said mask comprising first locations and second locations, said first locations substantially transparent to at least ultraviolet light and said second locations substantially opaque to at least ultraviolet light, said second locations comprising a light blocking material on a first surface of said mask, said first surface of said mask placed in contact with said glass plate,



5 e) ~~filling said reactor space with a reaction solution;~~

10 f) illuminating said mask with at least ultraviolet light, said ultraviolet light removing said photoprotective material from said at least a first surface of said glass plate under said first locations of said mask;

15 g) exposing said first surface to a first amino acid, said first amino acid binding to regions of said at least a first surface from which said photoprotective material was removed, said first amino acid comprising said photoprotective group at a terminus thereof;

20 h) placing a mask in contact with said glass plate at a second position;

25 i) illuminating said mask with at least ultraviolet light, said ultraviolet light removing said photoprotective material from said at least a first surface of said glass plate under said first locations of said mask;

30 j) exposing said at least a first surface to a second amino acid, said second amino acid binding to regions of said at least a first surface from which said photoprotective material was removed, said second amino acid comprising said photoprotective group at a terminus thereof;

35 k) placing a mask in contact with said glass plate at a third position;

40 l) illuminating said mask with at least ultraviolet light, said ultraviolet light removing said photoprotective material from said at least a first surface of said glass plate under said first locations of said mask;

45 m) exposing said at least a first surface to a third amino acid, said third amino acid binding to regions of said at least a first surface from which said photoprotective material was removed;

50 n) placing a mask in contact with said glass plate at a fourth position;

55 o) illuminating said mask with at least ultraviolet light, said ultraviolet light removing said photoprotective material from said at least a first surface of said glass plate under said first locations of said mask;

60 p) exposing said at least a first surface to a fourth amino acid, said fourth amino acid binding to regions of said at least a first surface from which said photoprotective material was removed, said at least a first surface comprising at least first, second, third, and fourth amino acid sequences;

65 q) exposing said at least a first surface to an antibody of interest, said antibody of interest binding more strongly to at least one of said first, said second, said third, or said fourth amino acid sequences;

r) exposing said at least a first surface to a receptor, said receptor recognizing said antibody of interest and binding at multiple locations thereof, said receptor comprising fluorescein;

5 s) exposing said at least a first surface to light, said first surface fluorescing in at least a region where said more strongly bound amino acid sequence is located; and t) detecting and recording fluoresced light intensity as a function of location across said at least a first surface.

10 70. A method of identifying at least one peptide sequence for binding with a receptor comprising the steps of:

a) on a substrate having a plurality of polypeptides, each having a photoremovable protective group, irradiating first selected polypeptides to remove said protective group;

15 b) contacting said polypeptides with a first amino acid to create a first sequence, second polypeptides on said substrate comprising a second sequence; and c) identifying which of said first or said second sequence binds with said receptor.

20 71. The method as recited in claim 70 wherein said step of identifying further comprises a step of detecting the presence of a marker selected from the group consisting of radioactive markers and fluorescent markers in said receptor.

25 72. The method as recited in claim 70 wherein said step of irradiating is a step of masking a light source with a mask, said mask comprising first transparent regions and second opaque regions.

73. The method as recited in claim 72 wherein the step of identifying further comprises the steps of:

30 a) exposing a first receptor to said substrate; and b) exposing a receptor to said first receptor to said substrate, said receptor to said first receptor comprising a marker.

74. The method as recited in claim 73 wherein said marker is selected from the group consisting of radioactive markers and fluorescent markers.

75. The method as recited in claim 73 wherein said first receptor is an antibody from a first species and said receptor to said first receptor is an antibody from a second species directed at said first species.

76. A method for screening a plurality of polymers for biological activity comprising exposing a receptor to a substrate having said plurality of said polymers on a surface thereof, each of said polymers occupying an area of less than about 1 cm².

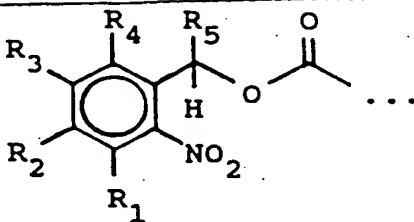
77. A method for screening as recited in claim 73 wherein said area is less than about 0.1 cm².

78. A method as recited in claim 73 wherein said area is less than about 10,000 μm^2 .

79. A method as recited in claim 73 wherein said area is less than about 100 μm^2 .

80. Apparatus for preparation of a plurality of polymers comprising:
a) a substrate with a surface, said surface comprising a reactive portion, said reactive portion activated upon exposure to an energy source so as to react with a monomer; and
b) means for selectively protecting and exposing portions of said surface from said energy source.

81. Apparatus as recited in claim 80 wherein said reactive portion further comprises a protective group, said protective group of the form:



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where R₁ is alkoxy, alkyl, halo, aryl, alkenyl, or hydrogen; R₂ is alkoxy, alkyl, halo, aryl, nitro, or hydrogen; R₃ is alkoxy, alkyl, halo, nitro, aryl, or hydrogen; R₄ is alkoxy, alkyl, hydrogen, aryl, halo, or nitro; and R₅ is alkyl, alkynyl, cyano, alkoxy, hydrogen, halo, aryl, or alkenyl.

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82. Apparatus as recited in claim 80 wherein said reactive portion further comprises linker molecules.

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83. Apparatus as recited in claim 82 wherein said linker molecules are selected from the group consisting of ethylene glycol oligomers, diamines, diacids, amino acids, and combinations thereof.

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84. Apparatus as recited in claim 80 wherein said means for selectively protecting further comprises a mask.

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85. Apparatus as recited in claim 80 wherein said means for selectively protecting further comprises a light valve.

source.

86. Apparatus as recited in claim 80 wherein said energy source is a light

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87. Apparatus as recited in claim 80 wherein said reactive portion further comprises a composition selected from the group consisting of nitroveratryloxy carbonyl, nitrobenzyloxy carbonyl, dimethyl-dimethoxybenzyloxy carbonyl, 5-bromo-7-nitroindolinyl, hydroxy-2-methyl cinnamoyl, and 2-oxymethylene anthraquinone.

88. Apparatus for preparation of a substrate having a plurality of amino acid sequences thereon, said apparatus comprising:

a) a substrate with a surface;

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- b) a protective group on said surface, said protective group removable upon exposure to an energy source, said energy source selected from the group consisting of light, electron beams, and x-ray radiation;
- c) means for directing said energy source at selected locations on said surface;
- d) means for exposing amino acids to said surface for binding to said surface.

10 89. Apparatus for screening polymers comprising a substrate with a surface, said surface comprising at least two predefined regions, said predefined regions containing different monomer sequences thereon, said predefined regions each occupying an area of less than about 0.1 cm^2 .

15 90. Apparatus as recited in claim 89 wherein said area is less than about 0.01 cm^2 .

91. Apparatus as recited in claim 89 wherein said area is less than 10000 μm^2 .

20 92. Apparatus as recited in claim 89 wherein said area is less than about $100 \mu\text{m}^2$.

93. Apparatus as recited in claims 89, 90, 91, or 92 wherein said monomer sequences are substantially pure within said predefined regions.

25 94. A substrate for screening for biological activity, said substrate comprising 10^3 or more different ligands on a surface thereof in predefined regions.

95. A substrate as recited in claim 94 wherein said substrate comprises 104 or more different ligands in predefined regions.

30 96. A substrate as recited in claim 94 wherein said substrate comprises 105 or more different ligands in predefined regions.

97. A substrate as recited in claim 94 wherein said substrate comprises 106 or more different ligands in predefined regions.

98. A substrate as recited in claims 94, 95, 96, or 97 wherein the ligands are peptides.

99. A substrate as recited in claim 89 wherein said ligands are substantially pure within said predefined regions.

100. Apparatus for screening for biological activity comprising:

a) a substrate comprising a plurality of poly-mer sequences, said polymer sequences attached to a surface of said substrate at known locations on said substrate, each of said sequences occupying an area of less than about 0.1 cm²;

b) means for exposing said substrate to a receptor, said receptor marked with a fluorescent marker, said receptor binding with at least one of said sequences; and

c) means for detecting a location of said fluorescent marker on said substrate.

101. Apparatus for forming a plurality of polymer sequences comprising:

a) a substrate, said substrate having at least a first surface and a second surface, said second surface comprising a photoremovable protective material, said substrate substantially transparent to at least light of a first wavelength;

b) a reactor body, said reactor body having a mounting surface with a reaction fluid cavity therein, said second surface maintained in a sealed relationship with said mounting surface; and

c) a light source for producing light of at least said first wavelength and directed at a surface of said substrate.

102. Apparatus as recited in claim 101 wherein said light source is directed at said first surface.

103. Apparatus as recited in claim 101 further comprising a mask, said mask placed between said light source and said first surface, said mask having first regions substantially transparent to said first wavelength of light and second regions substantially opaque to said first wavelength of light.

104. Apparatus as recited in claim 101 wherein said cavity comprises a fluid inlet and a fluid outlet, said fluid inlet connected to a pump for flowing reaction fluids through said cavity.

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105. Apparatus as recited in claim 101 wherein said cavity further comprises a plurality of raised sections.

106. Apparatus as recited in claim 103 wherein said mask further comprises a glass plate.

107. Apparatus as recited in claim 106 wherein said opaque regions on said mask comprise chrome.

15 108. Apparatus as recited in claim 101 wherein at least a portion of said second surface comprises a second photoremovable protective group, said second photoremovable protective group activatable upon exposure to light of a second wavelength.

20 109. Apparatus as recited in claim 101 further comprising first and second gaskets on said mounting surface and means for maintaining a vacuum between said first and second gaskets.

110. Apparatus as recited in claim 101 wherein said substrate has a thickness of less than 1 mm.

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111. Apparatus as recited in claim 101 wherein said substrate has a thickness of less than 0.5 mm.

30 112. Apparatus as recited in claim 101 wherein said substrate has a thickness of less than 0.05 mm.

113. Apparatus as recited in claim 103 wherein said mask is in direct contact with said substrate.

114. Apparatus as recited in claim 113 wherein opaque regions of said mask are placed in direct contact with said substrate.

115. Apparatus as recited in claim 101 further comprising a liquid crystal light valve for selectively controlling exposure of light to said substrate.

116. Apparatus as recited in claim 101 further comprising a fiber optic faceplate between said light source and said substrate.

117. Apparatus as recited in claim 101 further comprising a molecular microcrystal between said light source and said substrate.

118. Apparatus as recited in claim 101 wherein said cavity comprises light absorptive materials.

119. Apparatus as recited in claim 118 wherein said light absorptive material is N,N-diethylamino 2,4-dinitrobenzene.

120. Apparatus as recited in claim 101 wherein said cavity is filled with a carrier solution.

121. Apparatus as recited in claim 120 wherein said carrier material comprises a material selected from the group of 1-hydroxybenzotriazole, dimethylformamide, diisopropylethylamine, and benzotriazolyl-n-oxy-tris(dimethylamino)phosphoriumhexafluorophosphate.

122. Apparatus as recited in claim 101 wherein said substrate is a fiber optic faceplate.

123. Apparatus for detection of fluorescent marked regions on a substrate comprising:

- a) a light source for directing light at a surface of said substrate;
- b) a means for detecting light fluoresced from said surface in response to said

light source;

c) means for translating said substrate from a first position to a second position; and

d) means for storing fluoresced light intensity as a function of location on said substrate, said means for storing connected to said means for translating and said means for detecting.

124. Apparatus as recited in claim 123 further comprising video display means for displaying light intensity as a function of location on said substrate.

10 125. Apparatus as recited in claim 123 wherein said means for detecting
comprises a photomultiplier tube and a photon counter.

126. Apparatus as recited in claim 124 wherein said means for directing light further comprises a dichroic mirror, said mirror reflecting light at a wavelength of said 15 light source and passing said fluoresced light.

127. Apparatus as recited in claim 125 wherein said light source is a laser light source.

20 128. Apparatus as recited in claim 126 wherein said means for storing is a
programmed digital computer.

129. Apparatus as recited in claim 127 further comprising a microscope, said light source directed at said substrate through said microscope, said means for detecting receiving light from said microscope.

130. A method of identifying at least one polymer for binding with a receptor comprising the steps of:

30 a) on a substrate, said substrate comprising polymers immobilized on a surface of said substrate, said polymers comprising a photoremovable protective group, irradiating a first region of said substrate without irradiating a second region of said substrate to remove said protecting group from said polymers in said first region; and

b) contacting said substrate with a first monomer to couple said monomer to said polymer in said first region, forming a first polymer on said substrate in said first region that is different from said polymer in said second region.

5 131. The method as recited in claim 130 wherein said step of irradiating is a step of masking a light source with a mask, said mask comprising first transparent regions and second opaque regions, said transparent regions transmitting light from said source to said first regions, and said opaque regions blocking light from said source to said second regions.

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132. The method as recited in claim 130 wherein said first and second regions each have total areas less than about 1 cm².

15 133. The method as recited in claim 130 wherein said steps of irradiating are conducted with a monochromatic light.

20 134. The method as recited in claim 130 wherein said step of irradiating a first region is a step of masking a light source with a mask located in a first position, and wherein said step of irradiating a second region is a step of masking a light source with said mask located in a second position.

135. The method as recited in claim 130 wherein the step of irradiating further comprises the steps of:

25 a) placing a mask adjacent to said substrate, said mask having substantially transparent regions and substantially opaque regions at a wavelength of light; and

 b) illuminating said mask with a light source, said light source producing at least said wavelength of light.

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136. An array of oligonucleotides, the array comprising:
a planar solid support having at least a first surface; and
at least 1000 different oligonucleotides attached to the first surface of the solid
support in an areas of less than 1 cm², wherein each of the different oligonucleotides is
5 attached to the surface of the solid support in a different known location, and has a different
sequence.

137. The array of claim 136, wherein each different oligonucleotides is
from about 4 to about 20 nucleotides in length.

10 138. The array of claim 136, wherein each different oligonucleotide is at
least 12 nucleotides in length.

15 139. The array of claim 136, wherein each different oligonucleotide is 2-
100 nucleotides in length.

140. The array of claim 136, wherein the array comprises at least 1,000
different oligonucleotides attached to the first surface of the solid support.

20 141. The array of claim 136, wherein the array comprises at least 10,000
different oligonucleotides attached to the first surface of the solid support.

142. The array of claim 136, wherein each of the different known locations
is physically separated from each other of the known locations.

25 143. The array of claim 136, wherein said planar solid support is glass.

144. The array of claim 136, wherein said oligonucleotides are attached to
the first surface of the solid support through a linker group.

30 145. The array of claim 136, wherein the oligonucleotide in the different
known locations are at least 20% pure.

146. The array of claim 136, wherein the oligonucleotides in the different known locations are at least 50% pure.

147. The array of claim 136, wherein the oligonucleotide in the different known locations are at least 80% pure.

148. The array of claim 136, wherein the oligonucleotide in the different known locations are at least 90% pure.

149. The array of claim 136, wherein the oligonucleotides in the different known locations are of known sequences.

150. The array of claim 136, wherein said array is produced by a binary synthesis process, said process comprising the steps of:

15 providing a planar solid support, said solid support having a plurality of compounds immobilized on a surface thereof, said compounds having protecting groups coupled thereto; deprotecting a first portion of said plurality of compounds on said surface and not a second portion of said plurality of compounds; reacting said first portion of said plurality of compounds with a first component of said oligonucleotide; deprotecting at least a third portion of said plurality of compounds on said surface, said third portion comprising a fraction of said first portion of said plurality of compounds; reacting said at least third portion of said plurality of compounds with a second component of said oligonucleotide; and 25 optionally repeating said binary synthesis steps to produce said oligonucleotide array.

151. An array of nucleic acids, the array comprising:
a planar support having at least a first surface; and
at least 1000 different nucleic acids attached to the first surface of the solid support
30 within an area of 1 cm², wherein each of the different nucleic acids is attached to the surface of the solid support in a different known location, has a different determinable sequence.

152. The array of claim 151, wherein each different nucleic acid is at least 20 nucleotides in length.

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153. The array of claim 151, wherein the array comprises at least 1,000 different nucleic acids attached to the first surface of the solid support.

10 154. The array of claim 151, wherein the array comprises at least 10,000 different nucleic acids attached to the first surface of the solid support.

155. The array of claim 151, wherein each of the different known locations is physically separated from each of the other known locations.

10 156. The array of claim 151, wherein said planar solid support is glass.

15 157. The array of claim 151, wherein said nucleic acids are attached to the first surface of the solid support through a linker group.

158. The array of claim 151, wherein the nucleic acids in the different known locations comprise nucleic acids that are at least 20% pure.

20 159. The array of claim 151, wherein the nucleic acid in the different known locations comprise nucleic acids that are at least 50% pure.

160. The array of claim 151, wherein the nucleic acids in the different known locations are at least 80% pure.

25 161. The array of claim 151, the nucleic acids in the different known locations are at least 90% pure.

162. The array of claim 151, wherein said array is produced by a binary synthesis process, said process comprising the steps of:

30 providing a planar, solid support, said solid support having a plurality of compounds immobilized on a surface thereof, said compounds having protecting groups coupled thereto; deprotecting a first portion of said plurality of compounds on said surface and not a second portion of said plurality of compounds;

reacting said first portion of said plurality of compounds with a first reactant;

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-deprotecting at least a third portion of said plurality of compounds on said surface, said third portion comprising a fraction of said first portion of said plurality of compounds; reacting said at least third portion of said plurality of compounds with a second reactant; and optionally repeating said binary synthesis steps to produce said nucleic acid array--.

10 163. The array of claim 151, wherein the nucleic acids are covalently attached to the support.

15 164. An array of nucleic acids, the array comprising:
a planar support having at least a first surface; and
a plurality of different nucleic acids attached to the first surface of the solid support at a density exceeding 10,000 different nucleic acids/cm², wherein each of the different nucleic acids is attached to the surface of the solid support in a different known location, and has a different determinable sequence.

20 165. An array of nucleic acids, the array comprising:
a planar support having at least a first surface; and
a plurality of different nucleic acids attached to the first surface of the solid support at a density exceeding 400 different nucleic acids/cm², wherein each of the different nucleic acids is attached to the surface of the solid support in a different known location, has a different determinable sequence, wherein the surface and the support are made from different materials.

25 166. The array of claim 151, wherein the different known locations are square in shape.

167. The array of claim 151, wherein the substrate is glass.

30 168. The array of claim 151, wherein the substrate is silicon dioxide.

169. The array of claim 151, wherein the substrate is
-(poly)tetrafluoroethylene, -(poly)vinylidene difluoride, polystyrene or polycarbonate.

170. The method of claim 151, wherein the substrate is optically transparent.

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171. The array of claim 151, wherein the substrate is functionalized with
groups that attach to the plurality of different nucleic acids.

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